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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,064	08/02/2005	Pierre Michel Desmons		4877

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SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER

GANGLE, BRIAN J

ART UNIT	PAPER NUMBER
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1645

MAIL DATE	DELIVERY MODE
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03/21/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/529,064	DESMONS ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 February 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☒ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: Claim 15 has been added. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: 1-10.
Claim(s) withdrawn from consideration: 11-14.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

ADVISORY ACTION

The amendment filed on 2/15/2007 under 37 CFR 1.116, in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance and will not be entered because a new claim has been added without the cancellation of a corresponding number of claims.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 2 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for the reasons set forth in the previous office action.

The term "prevalent" in claim 2 is a relative term which renders the claim indefinite. The term "prevalent" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what proportion of individuals in a population must be infected with a particular serosubtype for that serosubtype to be "prevalent."

Applicant argues: that the claim has been amended to overcome said rejection.

Applicant's arguments have been fully considered and deemed non-persuasive.

Because the after-final amendment has not been entered, claim 2 still contains language that renders the claim vague and indefinite.

The specification does not provide a clear, specific, limiting definition of the term "prevalent." The use of the language "most prevalent (or possibly second or third or fourth prevalent..." renders the definition unclear. Does applicant intend the definition of prevalent to mean first, second, third or fourth prevalent? Does applicant intend that "prevalent" might be first, second, third or fourth prevalent, but could be something else?

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-9 under 35 U.S.C. 102(b) as being anticipated by Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That while Berthet teach multivalent bleb preparations, they do not teach a composition comprising blebs that are deficient in PorA in combination with blebs that are not deficient in PorA.

2. That the disclosure of CU-385 and H44/76, by Berthet, is not made in reference to a bleb preparation with blebs from both of these strains, but rather to a single bleb preparation that is immunoprotective against both of these strains.

3. That Berthet does not inherently disclose a composition comprising blebs that are deficient in PorA in combination with blebs that are not deficient in PorA because Berthet discloses combinations of serotypes that, while they do contain the strains CU-385 and H44/76 (which are deficient PorA and not deficient in PorA, respectively), these serotypes may contain other strains which do not have the same PorA content as CU-385 and H44/76. Therefore, the composition of Berthet does not necessarily and/or inevitably contain at least one bleb preparation that is deficient in PorA in combination with at least one bleb preparation that is not deficient in PorA.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding arguments 1-3, on page 36, Berthet discloses vaccine bleb preparations which contain a mixture of blebs from several subtype/serotypes, such as P1.15 and P1.7,16. Applicant is correct that, on page 35, Berthet refers to compositions that should be immunoprotective against strains CU-385 and H44/76. However, it is not accurate to state that said

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immunoprotective preparation is not a mixture. Berthet refers to the manufacture of a bleb vaccine that is produced using more than one process in order to optimize the preparation. This suggests that said vaccine contains a mixture, especially since the vaccine should be protective against multiple strains. Additionally, Berthet refers to vaccines containing blebs from multiple serotypes, including P1.15 and P1.7,16. While there are strains in addition to CU-385 and H44/76, which are encompassed by these serotype designations, the skilled artisan reading Berthet would clearly realize that vaccines containing blebs from multiple serotypes, including P1.15 and P1.7,16 should contain blebs from strains CU-385 and H44/76, since Berthet states that vaccines should be immunoprotective against these two strains. The fact that Berthet does not mention the PorA content of these strains is not relevant, as CU-385 is deficient in PorA and H44/76 is not deficient in PorA.

The rejection of claims 1-9 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Granoff *et al.* (PCT Publication WO 02/09643, 2/7/2002), is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That the examiner is incorrect in asserting that Granoff discloses vaccines that contain blebs from multiple strains of *Neisseria* and that Granoff discloses the "Norwegian vaccine" and mixtures containing blebs from strain CU-385.

2. That Granoff's disclosure of the Norwegian vaccine refers to a preparation containing blebs from a single strain of *Neisseria*.

3. That Granoff's reference to CU-385 is limited to its use in testing the sera of animals immunized with the CHORI vaccine.

4. That Figure 1 does not disclose strain CU-385, but only a strain of serosubtype P1.15, which includes strains other than CU-385.

5. That the examiner incorrectly asserts that Granoff discloses individual bleb vaccines that comprise CU-385, and that Figure 1 only discloses a strain of serosubtype P1.15, not CU-385.

6. That Granoff does not disclose any compositions containing mixtures that include blebs of serosubtype P1.15, much less CU-385. Applicant further argues that claims 1-9 are not

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drawn to mixtures of blebs from different strains, but to mixtures containing blebs that are deficient in PorA and blebs that are not deficient in PorA.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding arguments 1 and 2, contrary to applicant's assertion, it is clear that Granoff discloses vaccines containing blebs from multiple strains of *Neisseria* (see, for example, page 7, line 28 through page 8, line 12). It is also clear that Granoff discloses the Norwegian vaccine (page 5, lines 5-10). The examiner has not asserted that mixtures containing the Norwegian vaccine are disclosed.

Regarding arguments 1 and 3, applicant is correct that the discussion of CU-385 on pages 44 and 48 are in reference to the use of CU-385 in testing antisera, and that these pages do not disclose a mixture containing CU-385. However, this does not mean that Granoff lacks disclosure of CU-385, or that a combination of CU-385 with the Norwegian vaccine would be unobvious. Both a composition containing CU-385 and one containing H44/76 are disclosed as effective vaccines. According to MPEP 2144.06, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Regarding arguments 4 and 5, Figure 1 discloses a vaccine with the serosubtype B:4:P1.15, that was used in Cuba and Brazil from 1987-1991. Granoff, on page 14, refers to an OMV vaccine prepared by the Finley Institute in Cuba which has been given to millions of children in South America. It is clear from an examination of the art and the instant specification, that CU-385 (commonly referred to as the Cuban strain) is the strain referred to in Granoff on page 14 and in Figure 1.

Regarding argument 6, as stated previously, Granoff discloses vaccine compositions which contain a mixture of blebs from different strains. Granoff also discloses vaccines that individually comprise CU-385 and H44/76 (the Norwegian vaccine). While Granoff does not explicitly disclose the combination blebs from these two strains, it would have been obvious to combine them for the reasons previously set forth. It is understood that the claimed invention is not merely a combination of blebs from different strains, but of a combination of blebs that are

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deficient in PorA and blebs that are not deficient in PorA; however, the combination of CU-385 and H44/76 meets this limitation.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) in view of Lehmann *et al.* (APMIS 99:769-772, 1991), is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That, as discussed above, Berthet does not teach compositions that contain at least one bleb preparation that is deficient in PorA in combination with at least one bleb preparation that is not deficient in PorA.

2. That Berthet does not teach any vaccine compositions containing the strain CU-385.

3. That the examiner has relied on the instant specification for the teaching that CU-385 is deficient in PorA, which constitutes improper hindsight reasoning.

4. Lehman does not remedy any of the above failings.

Applicant's arguments have been fully considered and deemed non-persuasive.

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Regarding arguments 1 and 2, as discussed above, it is clear from reading Berthet, that vaccines containing blebs from multiple strains are disclosed; and that strains CU-385 and H44/76 have been contemplated.

Regarding arguments 3 and 4, the examiner has not relied upon any teachings in the instant specification for to provide reasons for combining references. The examiner is simply using the instant specification to point out that applicant regards CU-385 as a strain that is deficient in PorA. This is an inherent property of the strain, not a judgment made using hindsight reasoning. Furthermore, it is not required that it be recognized whether the compositions of the prior art contained a specific amount of PorA, only that the compositions actually contained the appropriate amounts. Therefore, it is not relevant whether it was recognized that CU-385 is deficient in PorA, or that H44/76 is not deficient in PorA. The fact that these strains had this characteristic means that any composition comprising blebs from these strains would necessarily meet the limitations of the instant claims. In addition, the test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and there is no requirement that the examiner have the same reasons for combining as applicant. As stated previously, it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). One would have had a reasonable expectation of success based on the success already shown with each of the components of the composition.

Conclusion

No claim is allowed.

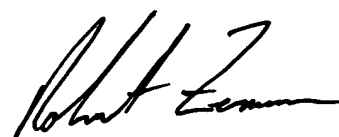
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brian Gangle
AU 1645


ROBERT A. ZEMAN
PRIMARY EXAMINER